

## Fanning the Flames: Low-Level Air Pollution and Risk of Surgery or Mortality for Persons with IBD

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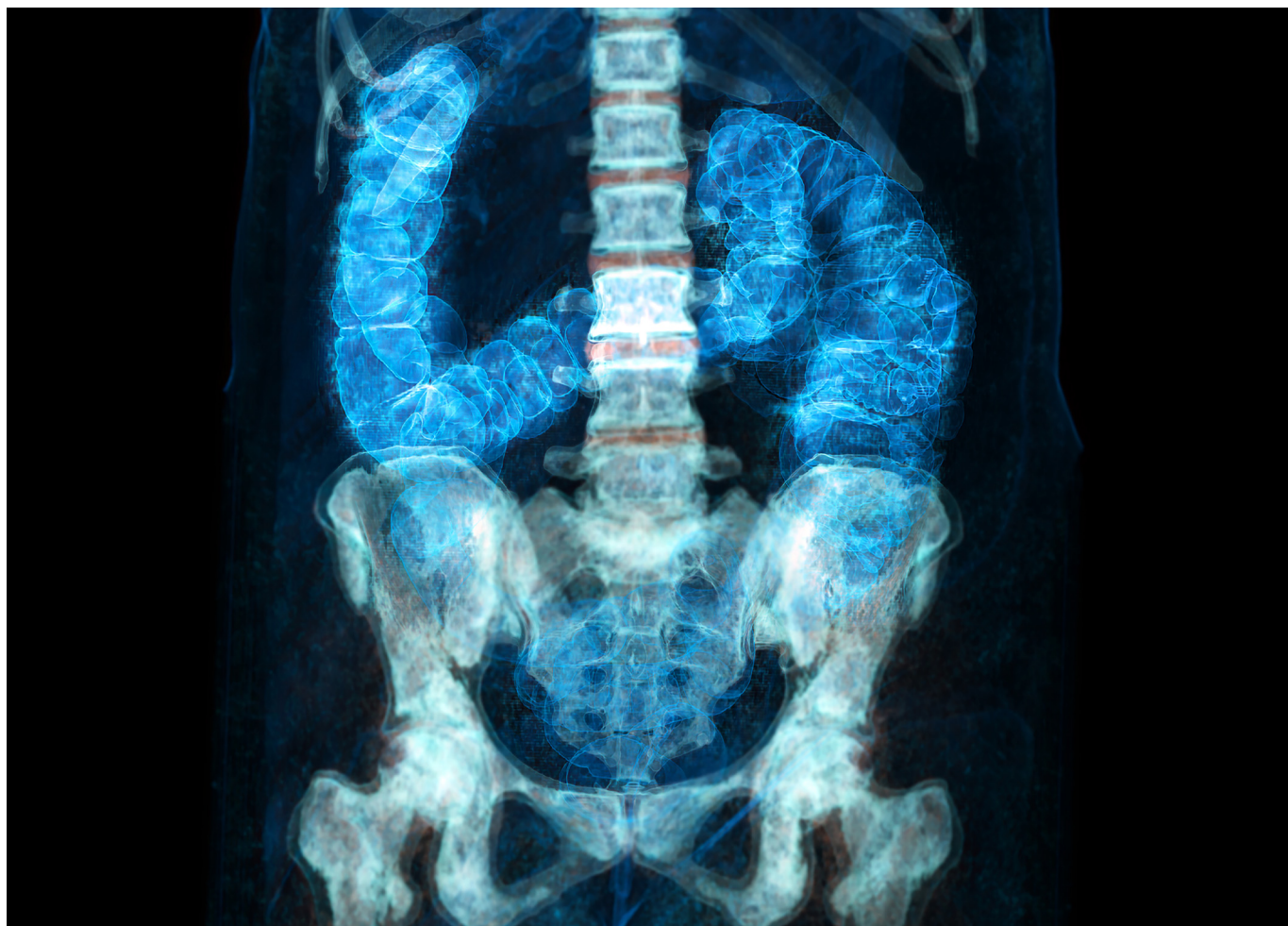
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Air pollution has been plausibly linked to the onset and worsening of inflammatory bowel disease (IBD),<sup>1</sup> yet little epidemiological or prospective evidence associates particular air pollutants with clinical outcomes.<sup>1–3</sup> The connection between air pollution and IBD—an immune-related disorder that includes both Crohn’s disease and ulcerative colitis—appears to involve an increase in inflammatory cytokines and damage to the glands and connective tissue that line the colon, called the colonic mucosa.<sup>1</sup> A new study in *Environmental Health Perspectives*<sup>4</sup> assessed whether concentrations of nitrogen oxides (NO<sub>x</sub>), nitrogen dioxide (NO<sub>2</sub>), and coarse and fine particulate matter (PM<sub>10</sub> and PM<sub>2.5</sub>, respectively) were associated with a person’s risk of gastrointestinal surgeries (or enterotomy), gastrointestinal cancer, and all-cause mortality.

“To our knowledge, the association between PM<sub>2.5</sub> and the risk of enterotomy among IBD patients has not been assessed by any

previous epidemiological study,” says co-corresponding author Xue Li, a professor at Zhejiang University School of Medicine in Hangzhou, China.

The research team used data from the UK Biobank, a national prospective cohort study that enrolled more than 500,000 people across the United Kingdom between 2006 and 2010. The researchers identified 4,708 participants who had IBD at baseline and whose residences had corresponding air pollution data. The team used average values of NO<sub>2</sub> and PM<sub>10</sub> over several years at the participants’ residences as a proxy measure for long-term exposure. For NO<sub>x</sub> and PM<sub>2.5</sub>, they used the only data available, which was collected in 2010, to analyze long-term exposure, reasoning that air pollution temporal trends were generally stable over this period. The team assessed diet and participants’ responses to food questionnaires, defining each person’s diet as either healthy or unhealthy.



Increases in exposure to NO<sub>x</sub> among study participants whose diets were scored as unhealthy were associated with increased risk of cancer in the gastrointestinal tract (including in the colon, shown here), Li says, compared with those who followed a cardioprotective diet. The findings suggest that inflammatory processes may play a role. Image: © Samunella/Science Source.

During the follow-up period, which averaged 12 years, the team found that increased exposure to PM<sub>2.5</sub> was associated with increased risk of gastrointestinal surgery and that increased exposures to PM<sub>2.5</sub>, as well as NO<sub>x</sub> and NO<sub>2</sub>, were associated with increased risk of all-cause mortality. After adjusting for the effects of socioeconomic status and lifestyle factors, the team estimated that a 1.3-μg/m<sup>3</sup> increase in PM<sub>2.5</sub> exposure was associated with a 16% increase in risk of gastrointestinal surgery and 14% increase in risk of all-cause mortality among participants.

Strong associations between increases in levels of each air pollutant and higher risk for gastrointestinal cancer appeared only after diet was factored in. “The large difference in the effect of air pollution on adverse outcomes between IBD patients following healthy and unhealthy diets is impressive,” adds Li, noting that these findings echo the team’s previous work.<sup>5</sup> Given that most participants did not live in high-pollution areas, Li says, “the dangers of low-level air pollution still cannot be ignored, especially for people with chronic diseases.”

The researchers also ran a mediation analysis, which Li says suggested that 5%–15% of the adverse effects of air pollution on enterotomy and all-cause mortality in IBD patients could be explained by elevated levels of systemic inflammation. Systemic inflammation was assessed using blood markers such as C-reactive protein, and counts of white blood cells, neutrophils, eosinophils, and platelets. The researchers speculate that the relatively low figure may be because the particular inflammatory factors induced by air pollution<sup>6</sup> were not among the factors assessed in the UK Biobank. “Air pollution may impair the prognosis of IBD patients through other pathways, including modulation of the gut microbiota and direct damage to the intestinal epithelium,”<sup>7</sup> she adds.

“The study is performed in subpopulations from a large prospective cohort, with high-quality data,” says Lu Qi, an epidemiology professor at Tulane University who was not involved in the study. “The findings add evidence to link air pollution to adverse events in IBD patients and suggest inflammation is a potential pathway of the effect, [highlighting] the importance of taking environmental factors into consideration in mitigating adverse events in IBD patients.”

Li noted some caveats. The study analyzed only individual air pollutants, not mixtures. In addition, the air pollutant measures available from the UK Biobank may not reflect long-term exposure levels, nor can baseline data on IBD predict long-term outcomes. Furthermore, she notes that the study population was mainly White and of European descent. “It is important to investigate the relations between air pollution and morbidity and mortality in IBD patients from other racial and ethnic groups,” Li says.

Ashwin Ananthakrishnan, a gastroenterologist and associate professor of medicine at Harvard Medical School, says many

concerns remain unanswered after the study. “The effect on mortality is interesting; however, a sizeable fraction of the deaths was cardio-respiratory in etiology, while the type of cancers leading to mortality and exact cause of mortality in such patients is not known,” he says. “Overall, this is consistent with the well-described adverse health effects of air pollution in the general population. To what degree any of these findings are specifically influenced by underlying IBD is less clear.” Ananthakrishnan would also like to see an adjustment for IBD-specific risk factors, including disease duration, clinical characteristics, and, importantly, impact of IBD treatment.

“Overall, our study highlights the important role of environmental health [specifically, reducing exposure to ambient air pollution] in improving the intermediate and long-term prognosis of IBD,” says Li. The work may also have practical implications, she says: “Can healthy diet be a possible option to address health threats from air pollution? A new research question is posed.”

**Wendee Nicole** is an award-winning science writer based in San Diego, CA, and a frequent contributor to *Environmental Health Perspectives*.

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